IN THE CLAIMS

Please amend claim 13 as shown below in clean form. Applicant attaches as Appendix B a set of Claim Amendments showing the specific text deletions as [bracketing], and text additions as underscoring.

A5

13 (Amended once). The process of claim 12, wherein the first solvent comprises at least one solvent selected from the group comprising dimethyl acetimide, n-methyl pyrrolidinone and tetrahydrofuran.

REMARKS

Claims 1-25 are pending and stand rejected. Claim 13 has been amended. The specification has been editorially amended. Reconsideration of the rejection is respectfully requested.

Applicant respectfully submits that the amendment to page 5 of the specification ("BRIEF DESCRIPTION OF THE DRAWINGS") adds no new matter to the application, but merely enhances clarity. Specifically, the word "microstructure" is used elsewhere in the specification, for example, on page 7, lines 15-23, where it can be seen to have a different context than that of the page 5 version.

Claims 1-25 were rejected under 35 U.S.C. 103 as being unpatentable over U.S. Patent No. 5,939,323 to Valentini et al. (hereinafter referred to as "Valentini") in view of U.S. Patent No. 5,019,096 to Fox, Jr. et al. (hereinafter referred to as "Fox Jr."), both further in view of U.S. Patent No. 5,024,671 to Tu (hereinafter referred to as "Tu"). Applicant respectfully traverses this rejection.

The Examiner appears to have captured the essence of the claimed invention. A polymer is dissolved in a first solvent, and then a second solvent is added that causes the solution of dissolved polymer to thicken to a gel consistency. The gel is then shape processed, e.g., molded, coated onto a substrate such as a suture, or bonded to another body to form a composite structure. The solvents are then removed, leaving behind a shaped porous polymer. At some point in the process, a biologically active agent optionally may be added. Among the many applications envisioned are medical applications such as vascular grafts.

Except for U.S. Patent No. 3,619,250 to Nishijima (hereinafter referred to as "Nishijima"), which seems to pertain to making synthetic leather, all of the cited references pertain to medical applications of polymeric materials.

Valentini discloses a technique for making a porous scaffold of a hyaluronic acid derivative that is useful in applications such as tissue repair, reconstruction and wound healing because the porous structure permits cell ingrowth. Simply stated, Valentini dissolves this hyaluronan based polymer in a first solvent, adds a leachable particle in sufficient quantity to make a

grainy paste, molds this paste to a desired shape, and then submerges this shaped paste into a large volume of a second solvent. The second solvent dissolves the leachable particle, i.e., the pore-forming agent, and extracts the first solvent, but is a "non-solvent with respect to the dissolved polymer. Thus, the polymer precipitates out of solution, leaving behind a porous scaffold that is biocompatible and biodegradable.

Fox Jr. discloses an infection resistant coating for various surfaces, particularly surfaces of medical devices. Specifically, a polymer such as polyurethane is dissolved in a first solvent such as THF to form a solution. An antimicrobial agent is dissolved in a second solvent that is miscible with the solution. The two solutions are then combined, the medical device is coated with the resulting composition, and allowed to dry (e.g., solvent removal by evaporation), leaving behind a polymeric coating containing antimicrobial agent.

Tu discloses a vascular graft featuring a tubular body formed from porous, biocompatible material, the tubular body including a layer of porous hollow fibers positioned along the inner surface. The graft may be prepared by winding fibers on a mandrel. A polymeric solution, such as polyurethane dissolved in THF, can be sprayed on the wound fibers to facilitate bonding between adjacent fibers. The polymer mixture will fill in between the adjacent fibers, thus decreasing the overall porosity of the graft (see, for example, column 6, lines 39-56).

The Examiner is correct that there are various deficiencies in the cited references. For the sake of simplicity, however, applicant focuses on one such deficiency, namely, the second or "gelling" solvent, and its significance to the claimed invention.

The Action stated that neither Valentini nor Fox Jr. discloses applicant's second solvent (sometimes interchangeably referred to as the "gelling solvent"), but that several examples of solvents that can be used as gelling solvents, such as p-dioxane, dimethyl sulfoxide and o-xylene, are disclosed by Nishijima, as is THF, an example of the first claimed solvent. The Action argues that it would have been obvious to a skilled artisan to use these compounds for the purpose of making a porous polymeric material from polyurethane.

Applicant respectfully traverses this position.

Applicant respectfully submits that while Nishijima certainly discloses both THF and dimethyl sulfoxide as solvents for polyurethane, Nishijima neither discloses nor suggests that dimethyl sulfoxide can be a gelling solvent for a solution of polyurethane in THF. This may be because Nishijima fails to appreciate that the dimethyl sulfoxide would have to be added <u>subsequent</u> to the dissolution of the polyurethane in THF for gelling to work. Instead, Nishijima suggests, at best, that the solvent for polyurethane could be a <u>mixture</u> of THF and dimethyl sulfoxide. As applicant has pointed out, however, when he attempted to dissolve polyurethane in a mixture of THF and dimethyl sulfoxide (e.g., gelling solvent), the polyurethane failed to dissolve. (See, for example, the Comparative Example.) He concluded that "addition sequence" can be important, and at least as far as dimethyl sulfoxide is

concerned, this particular gelling solvent needs to be added after the polymer is dissolved in the first solvent, THF.

As the Action has pointed out, Tu is silent as to a second solvent. Fox and Valentini each disclose two solvents for a polymer system, but they serve purposes different than the claimed second solvent. In Fox, the second solvent is for dissolving the antimicrobial agent. In Valentini, the second solvent extracts the first solvent and pore-forming agent. Applicant respectfully submits that one skilled in the art will readily recognize Valentini's disclosure as describing the simple phase separation/precipitation technique combined with a particulate leaching step that the claimed invention rejects. See, for example, page 6, lines 13-20 of the present application.

Applicant furthermore respectfully submits that none of the cited references discloses or suggests the gelling action that the second solvent can have upon the dissolved polymer. The ability to gel the polymer is important because a gel can be molded to produce fine detail in complex shaped articles such as a heart valve or a vascular graft having a branching feature, e.g., a "y graft". See, for example, Figure 14 and page 10, lines 39-47.

In view of the amendments and the above remarks, applicant respectfully submits that the present application is in condition for allowance. Accordingly, applicant respectfully requests issuance of a Notice of Allowance directed to claims 1-25.

Should the Examiner deem that any further action on the part of applicant would be desirable, the Examiner is invited to telephone applicant's undersigned representative.

Respectfully submitted,

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November 4, 2002

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Encl. Appendix A: Amendments to the specification in marked-up form
Appendix B: Amendments to the claims in marked-up form

Appendix A
Amendments to the specification in marked-up form

The second paragraph on page 2:

Compliance problems with woven polyethylene terephthalate and drawn out polytetrafluoroethylene prompted interest in thermoplastic elastomers for use as blood conduits. Medical grade polyurethane (PU) copolymers are an important member of the thermoplastic elastomer family. PU's are generally composed of short, alternating polydisperse blocks of soft and hard segment units. The soft segment is typically a polyester, polyether or a polyalkyldiol [polyalkyldoil] (e.g., polytetramethylene oxide). The hard segment is formed by polymerization of either an aliphatic or aromatic diisocyanate with chain extender (diamine or glycol). The resulting product containing the urethane or urea linkage is copolymerized with the soft segment to produce a variety of polyurethane formulations. PU's have been tested as blood conduits for over 30 years. Medical grade PU's, in general, have material properties that make it an excellent biomaterial for the manufacture of vascular grafts as compared to other commercial plastics. These properties include excellent tensile strength, flexibility, toughness, resistance to degradation and fatigue, as well as biocompatiblity. Unfortunately, despite these positive qualities, it became clear in the early 1980s that conventional ether-based polyurethane elastomers presented long-term biostabilty issues as well as some concern over potential carcinogenic degradation products. Further, in contrast to excellent performance in animal trials, clinically disappointing results with PU-based grafts diminished the attractiveness of the material for this application.

Please substitute the following "BRIEF DESCRIPTION OF THE DRAWINGS" for that of record:

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1-10 are Scanning Electron Microscope (SEM) images of four different vascular grafts made from four different species of polymer using the gel enhanced phase separation technique;

FIG. 11 is an optical photograph showing a pattern of tissue invasion into the porosity of the graft;

FIG 12 is a schematic illustration of the polymeric microscopic structure [microstructure] in the prior vascular grafts (right drawing) versus the polymeric microscopic structure [microstructure] in the vascular grafts of the present invention (left);

FIGS. 13a-13c show a possible embodiment of the present invention allowing for improved suturing; and

FIGS. 14a-14e[d] show various embodiments of the present invention made possible by the gel enhanced phase separation technique.

The paragraphs at the bottom of page 11:

3) The manufacturer identified dimethyl acetimide, n-methyl pyrrolidinone, and tetrahydrofuran as solvents for the polymer.
4) A 0.25-gram sample of polymer was placed into the bottom of 20 small bottles. Five milliliters of 20 common laboratory solvents, including the three listed by the manufacturer, was added to the bottles. The bottles were left for 48 hours at room temperature after which they were used to identify those solvents that dissolved or resulted in swelling of the polymer. Twelve solvents [polymers] were identified and are listed below along with freezing point ("F.P.", also known as melt point), boiling point ("B.P."), vapor pressure ("V.P."), and solvent group (S.G.). (Other properties that can aid in the selection of solvent and gelling solvent include, but are not limited to, density, molecular weight, refractive index, dielectric constant, polarity index, viscosity, surface tension, solubility in water, solubility in alcohol(s), residue, and purity.)

The paragraph at the top of page 13:

Sample B

Recognizing that dimethyl sulfoxide has a boiling point and vapor pressure unsuitable for freeze-drying, the Vial 13 gel is instead poured onto a Teflon tray, frozen at –15C and then submerged into a non-solvent (ethanol) at –10C for 12 hours to leach out the solvent and gelling solvent. (Had the gel been thick enough to form a stable gelatinous mass, freezing and the use of chilled alcohol would not be required.) The sheet was then removed from [form] the alcohol and soaked in distilled water 12 hours, after which it is dried and placed into a desiccator. The sheet formed was relatively stiff and had a non-fibrous porosity of greater than [that] 75%.

Appendix B

Amendments to the claims in marked-up form

13 (Amended once). The process of claim 12 [11], wherein the first solvent comprises at least one solvent selected from the group comprising dimethyl acetimide, n-methyl pyrrolidinone and tetrahydrofuran.